containers, aseptically transfer approximately 300 milligrams of sample into a sterile 500-milliliter Erlenmeyer flask containing approximately 400 milliliters of diluting fluid D. Add at least 200,000 Levy units[1] of penicillinase. Repeat the process using 10 additional containers. Swirl both of the stoppered flasks to completely solubilize the suspension prior to filtration and proceed as directed in paragraph (e)(1)(ii) of that section.

(3) *Pyrogens.* Proceed as directed in § 436.32(f) of this chapter, using a solution containing 20 milligrams of ampicillin per milliliter.

(4) [Reserved]

(5) *Loss on drying.* Proceed as directed in § 436.200(a) of this chapter.

(6) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 10 milligrams per milliliter.

(7) *Ampicillin content.* Proceed as directed in § 436.213 of this chapter, using both the titration procedures described in paragraph (e)(1) and (2) of that section. Calculate the ampicillin content as follows:

(i) *Acid titration.*

Percent ampicillin content=[(A − B) (normality of lithium methoxide reagent) (349.4) (100) (100)]/[(Weight of sample in milligrams) (100 − *m*)].

where:

A=Milliliters of lithium methoxide reagent used in titrating the sample;

B=Milliliters of lithium methoxide reagent used in titrating the blank;

m=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

Difference=(Potency in micrograms per milligram/10) − percent ampicillin content.

(ii) *Base titration.*

Percent ampicillin content=[(A − B) (normality of perchloric acid reagent) (349.4) (100) (100)]/[(Weight of sample in milligrams) (100 − *m*)].

where:

A=Milliliters of perchloric acid reagent used in titrating the samples;

B=Milliliters of perchloric acid reagent used in titrating the blank;

m=Percent moisture content of the sample.

Calculate the difference between the potency and the ampicillin content as follows:

Difference=(Potency in micrograms per milligram/10) − percent ampicillin content.

(8) *Crystallinity.* Proceed as directed in § 436.203(a) of this chapter.

(9) *Identity.* Proceed as directed in § 436.211 of this chapter, using a 0.5 percent potassium bromide disc, prepared as described in paragraph (b)(1) of that section.

[39 FR 18976, May 30, 1974, as amended at 46 FR 16683, Mar. 13, 1981; 49 FR 3458, Jan. 27, 1984; 50 FR 19918, May 13, 1985]

§ 440.8 Bacampicillin hydrochloride.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Bacampicillin hydrochloride is the hydrochloride salt of the 1–ethoxycarbonyloxyethyl ester of ampicillin. It is a white powder. It is so purified and dried that:

(i) Its potency is not less than 623 micrograms and not more than 727 micrograms of ampicillin per milligram on an ''as is'' basis.

(ii) [Reserved]

(iii) Its moisture content is not more than 1.0 percent.

(iv) Its pH in an aqueous solution containing 20 milligrams per milliliter is not less than 3.0 and not more than 4.5.

(v) It passes the identity test.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, moisture, pH, and identity.

(ii) Samples required: 10 packages, each containing approximately 300 milligrams.

(b) *Tests and methods of assay*—(1) *Potency.* Use either of the following methods; however, the results obtained from the iodometric assay shall be conclusive.

(i) *Hydroxylamine colorimetric assay.* Proceed as directed in § 442.40(b)(1)(ii) of this chapter, except:

[1] One Levy unit of penicillinase inactivates 59.3 units of penicillin G in 1 hour at 25° C. and at a pH of 7.0 in a phosphate buffered solution of a pure alkali salt of penicillin G when the substrate is in sufficient concentration to maintain a zero order reaction.

(*a*) *Buffer.* In lieu of the buffer described in § 442.40(b)(1)(ii) (*b*)(*2*) of this chapter, use the buffer prepared as follows: Dissolve 200 grams of primary standard tris (hydroxymethyl) aminomethane in sufficient distilled water to make 1 liter. Filter before use.

(*b*) *Preparation of working standard solution.* Use the ampicillin working standard. Dissolve and dilute an accurately weighed portion of the ampicillin working standard in sufficient distilled water to obtain a concentration of 1.25 milligrams of ampicillin per milliliter.

(*c*) *Preparation of sample solution.* Dissolve and dilute an accurately weighed portion of the sample with sufficient distilled water to obtain a concentration of 1.25 milligrams of ampicillin per milliliter (estimated).

(*d*) *Calculations.* Calculate the ampicillin content in micrograms per milligram as follows:

$$\text{Ampicillin content in micrograms per milligram} = \frac{A_u \times P_a}{A_s \times W_u}$$

(ii) *Iodometric assay.* Proceed as directed in § 436.204 of this chapter, except use the ampicillin working standard.

(2) [Reserved]

(3) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(4) *pH.* Proceed as directed in § 436.202 of this chapter, using an aqueous solution containing 20 milligrams per milliliter.

(5) *Identity.* Proceed as directed in § 436.330 of this chapter.

[46 FR 25603, May 8, 1981, as amended at 50 FR 19918, May 13, 1985]

§ 440.9a Sterile ampicillin sodium.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Sterile ampicillin sodium is the sodium salt of D(-)$_\alpha$-aminobenzyl penicillin. It is so purified and dried that:

(i) Its potency is not less than 845 micrograms and not more than 988 micrograms of ampicillin per milligram on an anhydrous basis. If it is packaged for dispensing, it contains not less than 90 percent and not more than 115 percent of the number of milligrams of ampicillin that it is represented to contain.

(ii) It is sterile.

(iii) It is nonpyrogenic.

(iv) [Reserved]

(v) Its moisture content is not more than 2 percent.

(vi) Its pH in an aqueous solution containing 10 milligrams per milliliter is not less than 8.0 and not more than 10.0.

(vii) Its ampicillin content is not less than 84.5 percent, except if the high-performance liquid chromatographic (HPLC) assay method is used, then the ampicillin content standard is not applicable.

(viii) The potency-base titration concordance is such that the difference between the potency value divided by 10 and the percent ampicillin content of the sample determined by the nonaqueous base titration is not more than 6, except if the HPLC assay method is used, then the concordance standard is not applicable.

(ix) It is crystalline.

(x) It passes the identity test for ampicillin sodium.

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on the batch for potency, sterility, pyrogens, moisture, pH, ampicillin content, concordance, crystallinity, and identity.

(ii) Samples required:

(*a*) If the batch is packaged for repacking or for use in manufacturing another drug:

(*1*) For all tests except sterility: 10 packages, each containing approximately 300 milligrams.

(*2*) For sterility testing: 20 packages each containing approximately 300 milligrams.

(*b*) If the batch is packaged for dispensing:

(*1*) For all tests except sterility: A minimum of 15 immediate containers or if each vial contains 250 milligrams or less of ampicillin a minimum of 24 vials.